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Major and minor subgroup profile of blood in patients receiving multiple transfusions and donors

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Abstract:

OBJECTIVE: It was aimed to profile the blood subgroups of our region and to reveal the prevalence of auto/alloimmune sensitization in patients who had to undergo multiple erythrocyte transfusions and to establish the sensitization profile by screening major and minor subgroups.

MATERIALS AND METHODS: In this study, the distribution of ABO and Rh system major subgroups was studied in 100 donor blood. As the patient group, 50 patients who received three or more red blood cell transfusions were included. In addition to this group, Kell, Lewis, Duffy blood group systems were studied.

RESULTS: According to the ABO system, 35% of the donors were in O, 33% in A, 17% in AB, and 15% in B. According to the Rh system, 75% is Dvi positive. Rh system is 99% e positive and 33% E positive in major subgroups and Kell1 positivity is 8%. In the patient group, 22% D(-) was determined compared to Rh blood group. Among the major subgroups of Rh, C was 68%, E was 14%, c was 76%, and e positivity was found to be 100%. The Kell1 negativity rate is 96%. The highest negativity was found in 86% Lea antigen in Lewis system, in 36% S antigen in MNS system, 34% Fyb antigen in Duffy system, and 24% Jka antigen in Kidd system. When inappropriate blood is given for any antigen, a double population is formed. The double negativities we detected in our study occurred as follows according to blood group systems: E 18%, C 12%, c 8%, Cw 2%, Kell 1 2%, M 8%, N 4%, S 18%, s 6%, Fya 8%, Jka 6%, Jkb 22%. Indirect Agglutination Test (IAT) was negative in all patients.

CONCLUSION: IAT negativity in all patient groups suggests that we do not develop alloimmunization, but the high rates of double population suggest a high risk of alloimmunization.

Keywords:

Alloimmunization, donor, red blood cell antigens, safe blood, transfusion medicine

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Objective

Blood transfusion is a tissue or even organ transplantation due to the variety of antigen antibodies the blood contains. Among the blood group antigens, ABO, Lewis, and P are carbohydrates and antigens such as Rh, Kell, Kidd, Duffy, and MNS are in protein structure. Antibodies develop against these carbohydrate and protein antigens for various reasons. Antibodies against carbohydrate antigens (ABO, Lewis, and P) are immunoglobulin (Ig) M-type antibodies that are widely found in nature. ABO system antibodies develop approximately 6 months after birth and these antibodies are called "natural antibodies." Antibodies that develop against protein antigens (Rh, Kell, Kidd, Duffy, and MNS) are IgG antibodies. For the development of IgG-type antibodies, the host must encounter foreign antigens for reasons such as pregnancy, blood transfusion, or transplantation.[1] In terms of Blood Banking and Transfusion Medicine, understanding blood group system antigens and the structural and functional properties of antibodies against these antigens is important for ensuring blood transfusion safety.

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Alloimmunization is observed in patients with multiple transfusions.[2,3] The risk of alloimmunization increases with the number of transfusions.[4] Antigen-specific antibodies are formed by alloimmunization when the person receives erythrocytes containing antigen not found in their own erythrocytes. These antibodies are called alloantibodies, in this case, alloimmunization. Alloantibodies are formed against erythrocyte antigens (D, C, c, e, Le, Leb, M, N, S, s, Fya, Fyb, Jka, and Jkb) in the individual and are of the IgG type and can pass through the placenta. They react with the relevant antigen at 37°C, cannot agglutinate directly, and form a hemolysis reaction.[5]

In this study, it was aimed to profile the blood subgroups of our region, to determine the prevalence of auto/alloimmune sensitization in the patient group who had to receive multiple erythrocyte transfusions, and to establish the sensitization profile by screening major and minor subgroups.

Materials and Methods

This prospective study was conducted at Sakarya University Training and Research Hospital Blood Bank between October 2019 and December 2019. ABO and Rh system major subgroups were screened in 100 healthy donor blood bags. Fifty patients who applied to the oncology, hematology, and pediatric hematology–oncology department and had at least three or more red blood cell (RBC) transfusions were included in the study. Before starting the study, ethical permission was obtained (Sakarya University Medical Faculty, Ethic Committee January 30, 2019, E1279) and the patients were informed about the study by the researcher. Written consent was obtained from the patients who agreed to participate in the study. The patients signed consent forms. The following tests were studied: Rh subgroups (c, C, e, E), Kell (Kell 1), Lewis (Lea, Leb), Duffy (Fya, Fyb), Kidd (Jka, Jkb), and MNS (M, N, S, s). Alloimmunization was screened by the indirect agglutination test (IAT). Samples taken from the patient group and healthy donor bag blood were studied without waiting. DAT was studied for all examples in this study.

Results

Of the 100 healthy donor parts of the study group, 33 (33%) were A, 15 (15%) were B, 17 (17%) were AB, and 35 (35%) were in the O group. Distribution of donors according to Rh major subgroup system was as follows: 75% Dvi (+) (Rh 1), 60% C (Rh 2), 33% E (Rh 3), 85% c (Rh 4), and 99% e (Rh 5) antigens positivity were detected. In addition, against Cw antigen, no positivity was observed in any donor. The positivity rate against Kell system antigen, Kell 1, is 8% [Table 1].

The patient group consisted of 64% of men and 36% of women. The distribution by age groups has been examined under three groups as 0–18 years old, 19–65 years old, and over 65 years old, and the distribution is given in Table 2. The average age of the patient group was found to be 47.9 ± 7.8.

The distribution of the patient group according to the history of receiving RBC transfusion was examined in four groups as 3–6 units, 7–10 units, 11–15 units, and over 15 units. It was determined that there were 14 patients receiving RBC transfusion between 3 and 6 units, 16 patients receiving 7–10 units, 12 patients receiving 11–15 units, and 8 patients receiving more than 15 units [Table 3].

D negativity was observed at a rate of 22% in the patient group compared to the Rh system blood group. One of the major subgroups of the Rh system of C (Rh 2) 20%, E (Rh 3) 68%, and c (Rh 4) 16% negativity was detected, and no negativity was observed in e (Rh5). Cw antigen

Table 1: ABO and rhesus major subgroup distribution of donors

RBC antigens	Positive numbers (*n*)
ABO system	
A	33
B	15
AB	17
0	35
RH system	
Dvı (+) (Rh 1)	75
C (Rh 2)	60
E (Rh 3)	33
c (Rh 4)	85
e (Rh 5)	99
Cw (Rh 8)	0
Kell system	
Kell (Kell 1)	8

RBC=Red blood cell, RH=Rhesus

Table 2: Distribution of patients by age groups

Age	Person, *n* (%)
0-18	13 (26)
19-65	19 (38)
<65	18 (36)
Total	50 (100)

Table 3: Distribution of patients receiving red blood cell transfusion

Number of transfusions	Patients, *n* (%)
3-6	14 (28)
7-10	16 (32)
11-15	12 (24)
<15	8 (16)
Total	50 (100)

negativity was observed in 98% of all patients. The rate of Kell 1 negativity, which is the Kell system antigen, is 96%. The Lewis system antigen Lea was 86% negative and Leb 2% negative. In the MNS system, the highest negativity was found in the S antigen with a rate of 36%, the highest negativity in the Fyb antigen with 34% in the Duffy system, and the highest negativity in the Jka antigen with 24% in the Kidd system [Table 4].

In the patient group, a double population was observed in the Rh (E, C, c, Cw), Kell (Kell 1), MNS (M, N, S, s), Duffy (Fya), and Kidd (Jka, Jkb) systems. Among the subgroups of the Rh system, 18% for the E (Rh 3) antigen, 2% for the Kell system antigen Kell 1, 18% for the S antigen most in the MNS system, 8% for the Fya antigen most in the Duffy system, and the most common Jkb antigens were 22% double population. No patients were observed double populations against Lewis system antigens [Figure 1].

Table 4: Negativity and double population rates of patients in Rh, Lewis, MNS, Duffy, and Kidd systems

RBC antigens	Negative (–), *n* (%)	DP, *n* (%)
Rh system		
Dvı (+) (Rh 1)	11 (22)	-
C (Rh 2)	10 (20)	6 (12)
E (Rh 3)	34 (68)	9 (18)
c (Rh 4)	8 (16)	4 (8)
e (Rh 5)	-	-
Cw (Rh 8)	49 (98)	1 (2)
Kell system		
Kell (Kell 1)	48 (96)	1 (2)
Lewis system		
Lea	43 (86)	-
Leb	1 (2)	-
MNS system		
M	7 (14)	4 (8)
N	9 (18)	2 (4)
S	18 (36)	9 (18)
S	4 (8)	3 (6)
Duffy system		
Fya	8 (16)	4 (8)
Fyb	17 (34)	-
Kidd system		
Jka	12 (24)	3 (6)
Jkb	16 (32)	11 (22)

RBC=Red Blood Cell, DP=Double population, Rh=Rhesus, MNS=MNS Blood group system

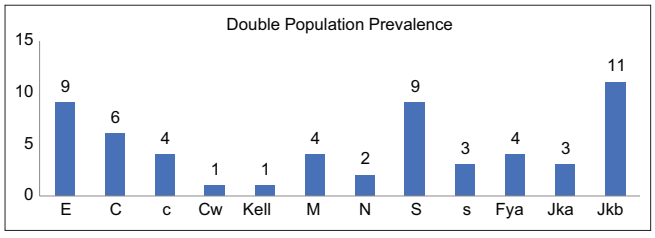

Figure 1: Distribution of double population

In the patient group, the IAT result we examined to determine the prevalence of alloimmunization was negative in all patients.

Discussion

Alloimmunization against RBC antigens occurs due to the genetic diversity of antigens between blood donors and recipients. Clinically significant antigen systems that trigger the development of IgG alloantibodies are Rhesus (Rh), Kell (Kell 1), Lewis (Lea, Leb), MNS (M, N, S, s), Duffy (Fya, Fyb), and Kidd (Jka, Jkb). Establishing the distribution profile of these antigens, especially in individuals exposed to multiple transfusions, decreases the rate of alloantibody formation and increases transfusion safety by preventing the formation of hemolytic reactions due to transfusion.[6]

The distribution rate of A, O, B, and AB blood groups worldwide was reported as 41%, 47%, 9%, and 3%, respectively. This rate is 37%, 47%, 12%, and 4% in America; 40%, 36%, 17%, and 7% in Bulgaria; 48%, 34%, 12%, and 6% in Greece; and in Turkey, 43%, 33%, 16%, and 8% were detected.[7] Similar rates were found in a study conducted in Kayseri in the Central Anatolia region.[8] While the B and O blood groups of our donor group in our study were close to the average of our country, the A blood type was found to be lower and the AB blood group to be higher.

Of the 13116 donors that Cekdemir *et al*. examined retrospectively between 2009 and 2013 in Sakarya, 44.3% were A group, 35.7% were O group, 12.5% were B group, and 7.5% were AB. It has been reported that the Rh Dvi (+) ratio is 84.9%.[9] According to the literature, among the data of our study, the rates of group A and Rh Dvi (+) were found to be lower, and the rates of group B were higher, and our AB and O group rates are similar to the literature.

In the study of Dogan *et al*., it was reported that among the Rh subgroup antigens, C 24.1%, E 70.5%, c 26.1%, and e 2.1% were negative.[10] In the Thailand study of Romphruk *et al*., it was reported that negativity was observed in e 3.2%, C 4.5%, c 65.6%, and E 67.8%.[11] In the study of Shah *et al*., among the Rh subgroup antigens, negativity C 9%, c 49.5%, E 83.5%, and e 0.5% were reported.[12] As can be seen, the negativity of c and E antigens is more common in the literature. In our study, while E negativity was parallel with the literature, C negativity was high, and c negativity was lower than the reported rates. The Turkish Red Crescent, which provides blood supply service for the East Marmara/West Black Sea region, should know that it is more important to provide E and C negative erythrocyte products.

It was reported that Kell 1 negativity in Turkey was 93.93% of the Kumas's study.[1] In our study, the Kell 1 antigen was found to be negative with a rate of 96% and it was found to be higher than the literature.

The Cw antigen was found to be 100% negative in the study performed by Kahar and Patel in 2014.[13] This situation is similar to the data of our study. For this reason, Duzce Regional Blood Center (Kocaeli, Sakarya, Duzce, Bolu, Zonguldak, Karabuk, and Bartin) serving the Western Black Sea should prepare all erythrocyte products negative in terms of Cw. Our findings in Turkey due to a lack of studies in the literature on Rh subgroups' distribution of blood donors in Turkey cannot be compared with the data. Our study will contribute to the literature on this subject.

In our study, the Rh Dvi (-) rate of the patient group is 22%. C antigen was detected as 20%, E antigen: 68%, c antigen: 16%, and Cw antigen: 98% negative, and no negativity was observed in the e antigen. As it is known, it is more important for the clinician to know which antigen of the patient is negative in terms of giving appropriate blood while performing transfusion. As a result of our study, the antigen negativities we found are as follows: Lea 86%, Leb 2%, M 14%, N 18%, S 36%, s 8%, Fya 16%, Fyb 34%, Jka 24%, Jkb 32%. The major blood group in Turkey, such as Cw, Kell 1, E, and C negative blood should be given. Transfusion should be done paying attention to negativity of Lea, S, Fyb, and Jkb from minor subgroups. This issue is a small number of scientific studies conducted in Turkey, revealing that the blood profiles of major and minor subgroups will contribute to the literature.

When inappropriate blood is given for any antigen, a double population is formed. The double negativities we detected in our study occurred as follows according to blood group systems: E 18%, C 12%, c 8%, Cw 2%, Kell 1 2%, M 8%, N 4%, S 18%, s 6%, Fya 8%, Jka 6%, Jkb 22%. In patients with highly negative subgroups, after transfusion of bag blood whose subgroup has not been determined, if the negative antigens of the patient are positive in the blood bag, it appears as a double population situation.

Studies have reported that providing leukocyte-filtered RBC transfusion reduces the risk of alloimmunization in patients receiving multiple transfusions.[14] Although naturally occurring non-ABO alloantibodies have been reported in volunteer blood donors, even in our patients, aloantibodies were not detected.[15] This situation showed that other studies to be conducted in a longer period are needed by increasing the sample size of the study. In our center, the use of leukocyte filters and irradiated blood in transfusion-dependent patients may cause us not to see alloimmunization.

The weakness of our study is that the detection of erythrocyte antigens was investigated only by serological methods. However, because of the high cost of molecular tests and exceeding our budget, they could not be used.

In some blood centers around the world, phenotype-matched erythrocyte transfusion is performed to reduce alloimmunization. However, the phenotype typing performed alone will not be sufficient due to the disadvantages of the result interpretation being subjective, the reliability of the kit, cell, and anti-serums used, and the difficulty in interpretation in the case of a double population, and the genotypes of the erythrocyte antigens can be revealed by the polymerase chain reaction-based genotyping method using individuals' DNA. However, the existence of a certain genotype does not guarantee that the antigen is present on the erythrocyte surface. Therefore, molecular tests should be seen as a complement to serological tests and should be applied together.[16] The weakness of our study is that the detection of erythrocyte antigens was investigated only by serological methods. However, because of the high cost of molecular tests and exceeding our budget, they could not be used. This study encouraged us to use flow cytometric and molecular methods in our future studies.

As a result, major and minor groups of blood should be studied in all patients with a transfusion-dependent diagnosis, and the use of subgroup appropriate blood should be increased further in addition to leukocyte-filtered and irradiated blood products to prevent alloimmunization that may develop in future. It has been emphasized that antigen negativities reported in the literature may not be valid for every region and that these should be revealed by local studies.

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Conflicts of interest

There are no conflicts of interest.

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